

**Part 1:** **TITLE, AUTHORS, APPROVALS, etc**

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| **Code assigned:** | **2022.001S.A** |  |
| **Short title:** Create a new family (*Noraviridae*), genus (*Orthonoravirus*) and species (*Orthonoravirus melanogastri*) in the order *Picornavirales*. | | |
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**List the ICTV Study Group(s) that have seen this proposal**

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**ICTV Study Group comments and response of proposer**

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**ICTV Study Group votes on proposal**

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| **Study Group** | **Number of members** | | |
| **Votes support** | **Votes against** | **No vote** |
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**Authority to use the name of a living person**

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| **Is any taxon name used here derived from that of a living person (Y/N)** | N |

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| **Taxon name** | **Person from whom the name is derived** | **Permission attached (Y/N)** |
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**Submission dates**

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| Date first submitted to SC Chair | 28 May 2022 |
| Date of this revision (if different to above) | 14 September 2022 |

**ICTV-EC comments and response of the proposer**

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**Part 2:** **NON-TAXONOMIC PROPOSAL**

**Text of proposal**

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**Part 3:** **TAXONOMIC PROPOSAL**

**Name of accompanying Excel module**

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| TP Proposal Excel module 20220528 |

**Abstract**

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| The proposed family *Noraviridae* is based on the previously described exemplar species, the Nora virus. *Noraviridae* forms a well-defined monophyletic clade that is firmly nested within the order *Picornavirales*, as evidenced from phylogenetic comparisons between encoded polymerase and helicase sequences. *Noraviridae* is on the other hand clearly distinct from other families in the order, with two extra open reading frames in its expanded genome, and with highly modified capsid proteins. The unique *Noraviridae* capsid can plausibly be construed as having evolved from a typical *Picornavirales* capsid, with modifications to encompass a larger genome. Besides the proposed exemplar species, *Orthonoravirus melanogastri*, RNA sequencing projects have disclosed several other putative members of *Noraviridae*. The phylogenetic relationship between these viruses tends to mimic that of their presumed hosts, suggesting that the *Noraviridae* are highly host-specific, and that they have only rarely crossed the species barriers during the past 400 million years. |

**Text of proposal**

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| |  | | --- | | The Nora virus was first discovered as a persistent infection in a *Drosophila melanogaster* lab stock, and it was later found to be commonly occurring in other lab stocks and in the wild. The infection has little or no effect on the life span or fecundity of the infected animals [2].  The *Drosophila melanogaster* Nora virus has a positive-sense, single-stranded RNA genome. The conserved polymerase and helicase sequences are similar to those of the *Picornavirales* families *Iflaviridae*, *Secoviridae*, *Picornaviridae* and *Dicistroviridae* (Fig. 1). There is also a region with similarity to picorna-like viral proteases, but it is not sufficiently conserved for unambiguous sequence alignment. Relatives of the Nora virus can be retrieved from various high-throughput transcriptomic and environmental projects. Based on a large number of RNA sequences, Shi *et al*. [6] proposed a *Nora-Virus-Related* clade that formed a well-supported sister group to the *Iflaviridae-and-Secoviridae-Related* clade (Fig. 2). In an exhaustive search of available databases [3], we identified a total of 17 viral RNAs with obvious sequence similarity to the *Drosophila melanogaster* Nora virus, forming a well-defined subgroup within the *Nora Virus Related* clade (Fig. 3A). We propose the name *Noraviridae*, at the family level, for this monophyletic group.  The placement of the proposed family *Noraviridae* in the order *Picornavirales* is well supported by the sequences of their replicative enzymes. Other features are unique, and distinctly different from other *Picornavirales*:  1. The genome is large, over 12 kb for the *Drosophila melanogaster* Nora virus, with typically four open reading frames (Fig. 4A). The replicative enzymes are encoded in the second open reading frame, which is relatively long [2]. The three major capsid proteins are encoded in the fourth open reading frame [1], in some cases interrupted by a frame shift between the individual protein sequences. The first and third open reading frames have no counterpart in other *Picornavirales*. They are poorly conserved, although the protein encoded in the third open reading frame has a conserved secondary structure with a long predicted coiled-coil region [5]. These characteristics make the *Noraviridae* different from other families in *Picornavirales*, as well as from the other members of the *Nora-Virus-Related* clade of Shi *et al*. [6] (Fig. 4B).  2. The *Noraviridae* capsid proteins lack detectable amino acid sequence similarity to those of other viruses (*i.e.* no significant blastp hits), including the other members of the *Nora-Virus-Related* clade. Yet, the capsid architecture is the same as in other members of the order *Picornavirales*, with a β-sheet jelly roll fold in all three capsid proteins. However, adjustments in the arrangement of the β-barrels causes an expansion of the capsid, allowing the encapsidation of the large genome [3]. Thus, the unique *Noraviridae* capsid can plausibly be construed as evolved from a typical *Picornavirales* capsid, with modifications to encompass a larger genome.  The host range of the proposed *Noraviridae* is largely confined to insects, and the phylogeny of the viruses tends to mimic that of their putative hosts (Fig. 3B). Exceptions are a few parasitic or predatory insects (and a spider) that harbor viruses that are closely related to the viruses of their prey, but it is not clear if the viruses are actively replicating in these parasites and predators, or if they were just ingredients in their last meal (however, the finding of a *Noraviridae*-like RNA in the transcriptome of a sea anemone is unexpected and requires further study). In any case, we can conclude that the viruses in the *Noraviridae* family have only rarely changed hosts during the past 400 million years, and that the viral family may be as old as the corresponding insect orders.  **Etymology.** Nora means ‘new’ in the Armenian language, and Nora virus was the name given when the virus was first described [2]. Because of its host specificity we propose to formally name the species *Orthonoravirus melanogastri*, after its host, *Drosophila melanogaster*. | |

**Supporting evidence**

See the enclosed file (Fig. 1-5.pdf).

**References**

1. Ekström J-O, Habayeb MS, Srivastava V, Kieselbach T, Wingsle G, Hultmark D (2011) *Drosophila* Nora virus capsid proteins differ from those of other picorna-like viruses. Virus Res 160:51-58

2. Habayeb MS, Ekengren SK, Hultmark D (2006) Nora virus, a persistent virus in *Drosophila*, defines a new picorna-like virus family. J Gen Virol 87:3045-3051

3. Laurinmäki P, Shakeel S, Ekström JO, Mohammadi P, Hultmark D, Butcher SJ (2020) Structure of Nora virus at 2.7 A resolution and implications for receptor binding, capsid stability and taxonomy. Sci Rep 10:19675

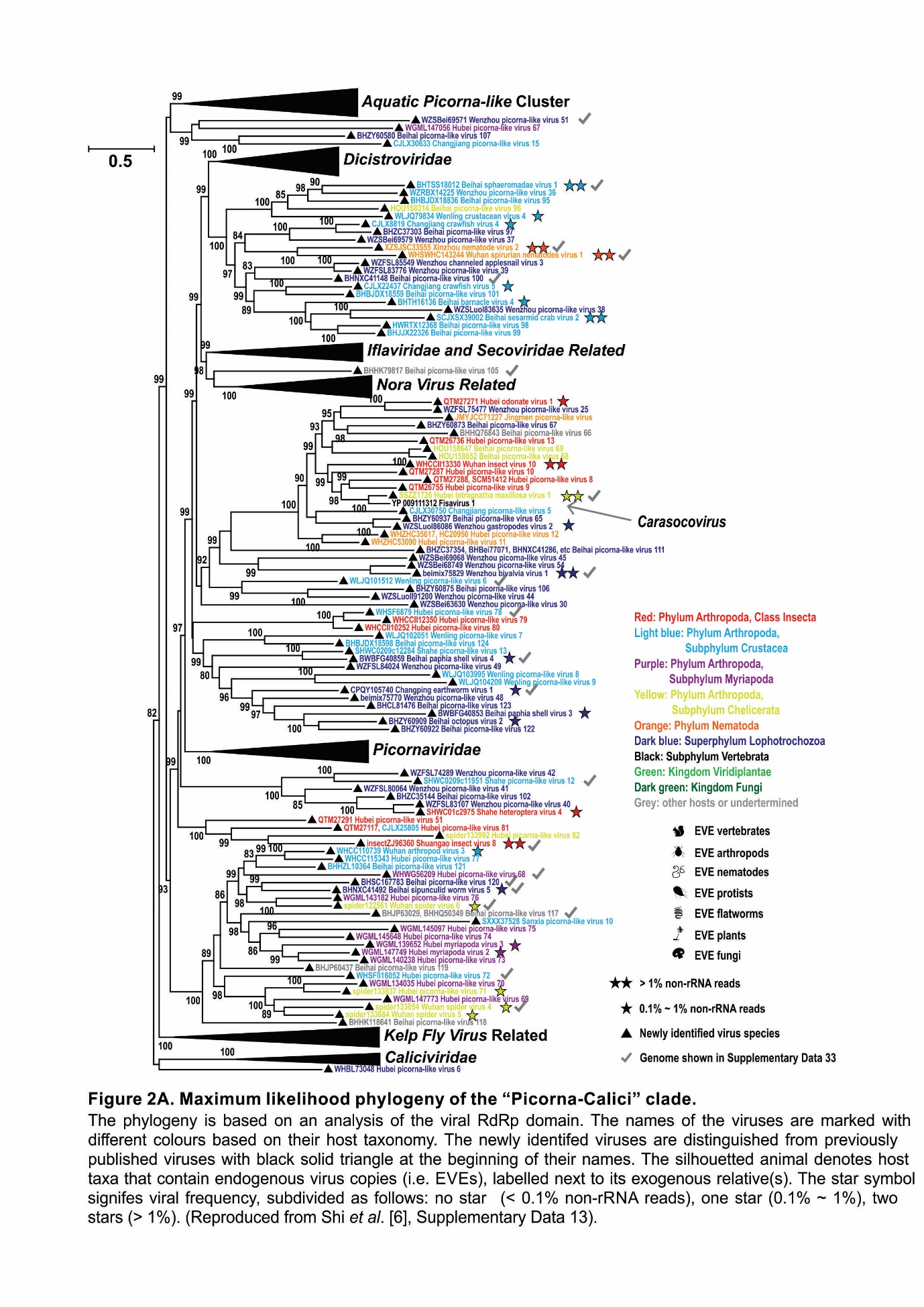
4. Misof, B. *et al.* Phylogenomics resolves the timing and pattern of insect evolution. *Science* **346**,763-767 (2014).

5. Sadanandan SA, Ekström J-O, Jonna VR, Hofer A, Hultmark D (2016) VP3 is crucial for the stability of Nora virus virions. Virus Res 223:20-27

6. Shi M, Lin XD, Tian JH, Chen LJ, Chen X, Li CX, Qin XC, Li J, Cao JP, Eden JS, Buchmann J, Wang W, Xu J, Holmes EC, Zhang YZ (2016) Redefining the invertebrate RNA virosphere. Nature 540:539–543

Diagram, schematic

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Diagram, schematic

Description automatically generated

Table

Description automatically generated with medium confidence

Chart, letter

Description automatically generated with medium confidence

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